

## **IMPLANT SURFACE PREPARATION**

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Date of Deposit: 2-27-96

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## IMPLANT SURFACE PREPARATION

### Cross Reference To Related Application

This application is a continuation-in-part of pending U.S. patent application Serial No. 08/351,214, filed November 30, 1994, for "Implant Surface Preparation."

### Field Of The Invention

The present invention relates to processes for improving the surfaces of devices to be surgically implanted in living bone, and to implant devices having the improved surfaces.

### Background Of The Invention

5       The success of prosthetic devices surgically implanted in living bone depends substantially entirely on achieving and maintaining an enduring bond between the confronting surfaces of the device and the host bone. Surgical procedures for preparing living bone to receive a surgically implanted prosthetic device have been known for twenty years or more, but considerable controversy remains concerning 10      the ideal properties of the surface of the device which confronts the host bone.

It is known through clinical experience extending over several decades that titanium and its dilute alloys have the requisite biocompatibility with living bone to be acceptable materials for use in making surgically implantable prosthetic devices, when the site of installation is properly prepared to receive them. There is, however, 15      less certainty about the ideal physical properties of the surfaces of the prosthetic devices which confront the host bone. For example, the endosseous dental implant made of titanium enjoys sufficient predictable success to have become the artificial root most frequently chosen for restoring dentition to edentulous patients, but that success depends in part on the micromorphologic nature of the surface of the implant 20      which comes in contact with the host bone. Because there is no standard for the surface micromorphology of dental implants, the surfaces of commercial implants have a wide range of available textures. It is known that osseointegration of dental implants is dependent, in part, on the attachment and spreading of osteoblast-like cells on the implant surface. It appears that such cells will attach more readily to

rough surfaces than to smooth surfaces, but an optimum surface for long-term stability has not yet been defined.

Wilke, H.J. et al. have demonstrated that it is possible to influence the holding power of implants by altering surface structure morphology: "The Influence of Various Titanium Surfaces on the Interface Strength between Implants and Bone", *Advances in Biomaterials*, Vol. 9, pp. 309-314, Elsevier Science Publishers BV, Amsterdam, 1990. While showing that increased surface roughness appeared to provide stronger anchoring, these authors comment that it "cannot be inferred exclusively from the roughness of a surface as shown in this experiment. Obviously the shear strength is also dependent on the kind of roughness and local dimensions in the rough surface which can be modified by chemical treatment."

Buser, D. et al., "Influence of Surface Characteristics on Bone Integration of Titanium Implants", *Journal of Biomedical Materials Research*, Vol. 25, pp. 889-902, John Wiley & Sons, Inc., 1991, reports the examination of bone reactions to titanium implants with various surface characteristics to extend the biomechanical results reported by Wilke et al. The authors state that smooth and titanium plasma sprayed ("TPS") implant surfaces were compared to implant surfaces produced by alternative techniques such as sandblasting, sandblasting combined with acid treatment, and plasma-coating with HA. The evaluation was performed with histomorphometric analyses measuring the extent of the bone-implant interface in cancellous bone. The authors state, "It can be concluded that the extent of bone-implant interface is positively correlated with an increasing roughness of the implant surface."

Prior processes that have been used in attempts to achieve biocompatible surfaces on surgically implantable prosthetic devices have taken many forms, including acid etching, ion etching, chemical milling, laser etching, and spark erosion, as well as coating, cladding and plating the surface with various materials, for example, bone-compatible apatite materials such as hydroxyapatite or whitlockite or bone-derived materials. Examples of U. S. patents in this area are 3,855,638 issued to Robert M. Pilliar 12/24/74 and 4,818,559 issued to Hama et al. 04/04/89. A process of ion-beam sputter modification of the surface of biological implants is

described by Weigand, A. J. et al. in *J. Vac. Soc. Technol.*, Vol. 14, No. 1, Jan/Feb 1977, pp. 326-331.

As Buser et al. point out (*Ibid* p. 890), the percentage of bone-implant contact necessary to create sufficient anchorage to permit successful implant function as a load-bearing device over time remains unclear. Likewise, Wennerberg et al., "Design and Surface Characteristics of 13 Commercially Available Oral Implant Systems", *Int. J. Oral Maxillofacial Implants* 1993, 8:622-633, show that the different implants studied varied considerably in surface topography, and comment: "Which of the surface roughness parameters that will best describe and predict the outcome of an implant is not known" (p. 632).

Radio-frequency glow-discharge treatment, also referred to as plasma-cleaning ("PC") treatment, is discussed in Swart, K. M. et al., "Short-term Plasma-cleaning Treatments Enhance in vitro Osteoblast Attachment to Titanium", *Journal of Oral Implantology*, Vol. XVIII, No. 2 (1992), pp. 130-137. These authors comment that gas plasmas may be used to strip away organic contaminants and thin existing oxides. Their conclusions suggest that short-term PC treatments may produce a relatively contaminant-free, highly wettable surface. U. S. Patents No. 5,071,351, issued December 10, 1991, and No. 5,188,800, issued February 23, 1993, both owned by the assignee of the present application, describe and claim methods and means for PC cleaning of a surgical implant to provide a contact angle of less than 20 degrees.

Copending application Serial No. 08/149,905, filed November 10, 1993, owned by the assignee of the present application, describes and claims inventions for improving the surfaces of surgically implantable devices which employ, among other features, impacting the surface with particles of the same material as the device to form the surface into a desired pattern of roughness.

#### Summary Of The Invention

It is a primary object of the present invention to produce an implant surface having a roughness that is substantially uniform over the area of the implant that is intended to bond to the bone in which the implant is placed.

It is a further object of this invention to provide an improved surgically implantable device having on its surface a substantially uniform micromorphology.

It is another object of the invention to provide a process or processes for manufacturing such improved implant devices.

It is an additional object of the invention to provide such improved implant devices which can be manufactured without contaminating the surfaces thereof.

5 It is a more specific object of the invention to provide an improved etch-solution process that will result in a substantially uniform surface topography on surgically implantable devices.

In accordance with the present invention, the foregoing objectives are realized by removing the native oxide layer from the surface of a titanium implant to provide  
10 a surface that can be further treated to produce a substantially uniform surface texture or roughness, and then performing a further, and different, treatment of the resulting surface substantially in the absence of unreacted oxygen. The removal of the native oxide layer may be effected by any desired technique, but is preferably effected by immersing the implant in hydrofluoric acid under conditions which remove the native  
15 oxide quickly while maintaining a substantially uniform surface on the implant. The further treatment is different from the treatment used to remove the native oxide layer and produces a desired uniform surface texture, preferably acid etching the surface remaining after removal of the native oxide layer. To enhance the bonding of the implant to the bone in which it is implanted, a bone-growth-enhancing material, such  
20 as bone minerals, hydroxyapatite, whitlockite, or bone morphogenic proteins, may be deposited on the treated surface. The implant is preferably maintained in an oxygen-free environment following removal of the native oxide layer, in order to minimize the opportunity for oxide to re-form before the subsequent treatment is performed.

#### Brief Description Of The Drawings

25 FIG. 1 is a diagrammatic sectional view taken through a body of titanium covered with a layer of native oxide;

FIG. 2 is the same section shown in FIG. 1 after impacting the surface with a grit;

30 FIG. 3 is the same section shown in FIG. 2 after bulk etching with an acid etch;

FIG. 4 is the same section shown in FIG. 2 after first removing the native oxide and then bulk etching with an acid;

FIGS. 5A and 5B are scanning electron micrographs ("SEMs") of two titanium dental implants prepared in accordance with the present invention;

5 FIGS. 6A and 6B are SEMs of the same implants shown in FIGS. 5A and 5B, at a higher magnification level;

FIG. 7 is a graph of the results of an Auger electron spectroscopic analysis of a titanium surface that has been exposed to air;

10 FIGS. 8A and 8B are SEMs of two titanium dental implants prepared in accordance with the present invention; and

FIGS. 9A and 9B are SEMs of the same implants shown in FIGS. 8A and 8B, at a higher magnification level.

#### Detailed Description Of The Preferred Embodiments

Turning now to the drawings, and referring first to FIG. 1, a titanium body 10 which has been exposed to air has on its outer surface 12 an irregular layer 14 of an oxide or oxides of titanium which form naturally. This oxide layer 14 is referred to herein as the "native oxide" layer, and typically has a thickness in the range from about 70 to about 150 Angstroms. The native oxide layer that forms naturally on titanium when it is exposed to air is actually a combination of different oxides of titanium, including  $TiO$ ,  $TiO_2$ ,  $Ti_2O_3$  and  $Ti_3O_4$ . The concentration of these oxides in the titanium body diminishes with distance from the surface of the body. The oxide concentration may be measured in an Auger spectrometer.

25 Auger electron spectroscopy (AES) measures the energy of Auger electrons produced when an excited atom relaxes by a radiationless process after ionization by a high energy electron, ion or x-ray beam. The spectra of a quantity of electrons emitted as a function of their energy reveal information about the chemical environment of the tested material. One of the major uses of AES is the depth profiling of materials, to reveal the thickness (depth) of the oxide layer on the surfaces of materials. These Auger electrons lie in an energy level that extends generally between the low energy level of the emission of secondary electrons up to the energy of the impinging electron beam. In this region, small peaks will occur in

the spectra at certain energy levels that identify the existence of certain elements in the surface.

As used herein, the term "native oxide layer" refers to the layer which extends from the surface of the material to the depth at which the energy of the peak-to-peak oxygen profile as measured in an Auger electron spectrometer decreases by one-half. For example, in the peak-to-peak oxygen profile reproduced in FIG. 7, the thickness of the native oxide layer was 130 Angstroms, which is the depth at which the oxygen profile dropped to half its maximum intensity. Thus, removal of a 130-Angstrom layer from the surface of the titanium body would remove the native oxide layer.

FIG. 2 depicts the surface 12 of the titanium body 10 after being grit blasted to achieve initial roughening, as described in more detail below. The oxide layer 14 is still present, but it has a rougher surface than in its original state depicted in FIG. 1.

FIG. 3 depicts the grit-blasted surface 12 of the titanium body 10 after it has been bulk etched in an etching acid. The etched area 16 where the native oxide layer 14 has been removed by the etching acid exhibits a much finer roughness, but in areas where the oxide layer remains, the initial roughness depicted in FIG. 2 also remains.

FIG. 4 depicts the grit-blasted surface 12 of the titanium body 10 after it has been etched in a first acid to remove the native oxide layer 14, and then in a second acid to produce the desired topography on the surface 16 produced by the first acid treatment. As described in more detail below, the preferred surface topography has a substantially uniform, fine roughness over the entire surface 16.

Among the processes previously used to improve the surfaces of dental implants made of titanium is that of etching the surface with an acid, such as a mixture of two parts (by volume) sulfuric acid and one part (by volume) muriatic acid. It has been found that such acid treatments do not etch an oxidized implant surface uniformly or consistently from one region to another.

According to one aspect of the present invention, the native oxide layer is removed from the surface of a titanium implant prior to the final treatment of the surface to achieve the desired topography. After the native oxide layer is removed, a

further and different 'treatment of the surface is carried out in the absence of unreacted oxygen to prevent the oxide layer from re-forming until after the desired surface topography has been achieved. It has been found that this process permits the production of unique surface conditions that are substantially uniform over the  
5 implant surface that is so treated.

Removal of the native oxide layer can be effected by immersing the titanium implant in an aqueous solution of hydrofluoric (HF) acid at room temperature to etch the native oxide at a rate of at least about 100 Angstroms per minute. A preferred concentration for the hydrofluoric acid used in this oxide removal step is 15%  
10 HF/H<sub>2</sub>O. This concentration produces an etch rate of approximately 200 - 350 Angstroms per minute at room temperature, without agitation, so that a typical native oxide layer having a thickness in the range from about 70 to about 150 Angstroms can be removed in about one-half minute. Other suitable etching solutions for removing the native oxide layer, and their respective etch rates, are:  
15

50% HF - etch rate ~ 600 to 750 Angstroms/min.

30% HF - etch rate ~ 400 to 550 Angstroms/min.

10% HF - etch rate ~ 100 to 250 Angstroms/min.

A 100% HF was found to be difficult to control, and the etch rate was not determined. The preferred 15% HF solution allows substantially complete removal  
20 of the native oxide layer with minimum further consumption of the titanium surface after the implant is removed from the solution.

The native oxide layer may be removed by the use of other acids, or by the use of techniques other than acid etching. For example, the Swart et al. article cited above mentions the use of plasma cleaning to remove thin oxides. Regardless of  
25 what technique is used, however, it is important to remove substantially all the native oxide from the implant surface that is intended to interface with the living bone, so that the subsequent treatment of that surface produces a substantially uniform surface texture to promote uniform bonding to the living bone. The native oxide layer is preferably removed from substantially the entire bone-interfacing surface of the  
30 implant. In the case of screw-type dental implants,<sup>such as implant 10, illustrated in FIG. 10,</sup> the bone-interfacing surface typically includes the entire implant surface beyond a narrow collar region<sup>12</sup> on the side wall of the implant at the gingival end thereof. This narrow collar region<sup>14</sup> preferably

- includes the first turn of the threaded portion of the implant. It is preferred not to etch the gingival end itself, as well as the narrow collar region, because these portions of the implant are normally fabricated with precise dimensions to match abutting components which are eventually attached to the gingival end of the implant.
- 5 Moreover, it is preferred to have a smooth surface on that portion of a dental implant that is not embedded in the bone, to minimize the risk of infection.

The treatment that follows removal of the native oxide layer must be different from the treatment that is used to remove the native oxide layer. A relatively aggressive treatment is normally required to remove the oxide layer, and such an aggressive treatment does not produce the desired uniform surface texture in the resulting oxide-free surface. Thus, after the native oxide layer has been removed, the resulting implant surface is immediately rinsed and neutralized to prevent any further attack on the implant surface. The surface is then subjected to the further, and different, treatment to produce a desired uniform surface texture. For example, 10 the preferred further treatment described below is a relatively mild acid-etching treatment which forms a multitude of fine cone-like structures having relatively uniform, small dimensions. Because of the prior removal of the native oxide layer, even a mild second treatment of the implant surface can produce a substantially 15 uniform effect over substantially the entire bone-interfacing surface of the implant.

Prior to removing the native oxide layer, the oxide-bearing surface may be grit blasted, preferably with grit made of titanium or a dilute titanium alloy. As is taught in the aforementioned copending U.S. patent application Serial No. 20 08/149,905, the use of a grit made of titanium avoids contaminating the surface of a titanium implant. Thus, for a dental implant made of commercially pure ("CP") 25 titanium, the blasting material may be CP B299 SL grade titanium grit. The preferred particle size for this grit is in the range from about 10 to about 60 microns (sifted), and the preferred pressure is in the range from about 50 to about 80 psi.

The surface treatment that follows removal of the native oxide layer from the implant surface may take several forms, singly or in combination. The preferred 30 treatment is a second acid etching step, using an etch solution ("Modified Muriaticetch") consisting of a mixture of two parts by volume sulfuric acid (96% by weight H<sub>2</sub>SO<sub>4</sub>, 4% by weight water) and one part by volume hydrochloric acid (37%

by weight HCl, 63% by weight water) at a temperature substantially above room temperature and substantially below the boiling point of the solution, preferably in the range from about 60°C. to about 80°C. This mixture provides a sulfuric acid/hydrochloric acid ratio of about 6:1. This preferred etch solution is controllable,  
5 allowing the use of bulk etch times in the range from about 3 to about 10 minutes. This solution also can be prepared without the risk of violent reactions that may result from mixing more concentrated HCl solutions (e.g., 98%) with sulfuric acid. This second etching treatment is preferably carried out in the absence of unreacted oxygen, and before the implant surface has been allowed to re-oxidize, following  
10 removal of the native oxide layer. Of course, the implants may be kept in an inert atmosphere or other inert environment between the two etching steps.

The second etching step produces a surface topography that includes many fine projections having a cone-like aspect in the sub-micron size range. Because of the fine roughness of the surface, and the high degree of uniformity of that roughness over the treated surface, the surface topography produced by this process is well suited for osseointegration with adjacent bone. As illustrated by the working examples described below, the final etched surface consists of a substantially uniform array of irregularities having peak-to-valley heights of less than about 10 microns. Substantial numbers of the irregularities are substantially cone-shaped elements  
15 having base-to-peak heights in the range from about 0.3 microns to about 1.5 microns. The bases of these cone-shaped elements are substantially round with diameters in the range from about 0.3 microns to about 1.2 microns, and spaced from each other by about 0.3 microns to about 0.75 microns. The SEMs discussed below, and reproduced in the drawings, illustrate the surface topography in more detail.  
20

25 The acid-etched surface described above also provides a good site for the application of various materials that can promote bonding of the surface to adjacent bone. Examples of such materials are bone-growth-enhancing materials such as bone minerals, bone morphogenic proteins, hydroxyapatite, whitlockite, and medicaments. These materials are preferably applied to the etched surface in the form of fine  
30 particles which become entrapped on and between the small cone-like structures. The bone-growth-enhancing materials are preferably applied in the absence of oxygen, e.g., using an inert atmosphere.

5       The roughness of the surface to which these materials are applied enhances the adherence of the applied material to the titanium implant. The uniformity of the rough surface enhances the uniformity of the distribution of the applied material, particularly when the material is applied as small discrete particles or as a very thin film.

10      A preferred natural bone mineral material for application to the etched surface is the mineral that is commercially available under the registered trademark "BIO-OSS". This material is a natural bone mineral obtained from bovine bone; it is described as chemically comparable to mineralized human bone with a fine, crystalline biological structure, and able to support osseointegration of titanium fixtures.

The invention will be further understood by reference to the following examples, which are intended to be illustrative and not limiting:

EXAMPLE NO. 1

15      A batch of 30 screw-type cylindrical implants made of CP titanium were grit blasted using particles of CP B299 SL grade titanium grit having particle sizes ranging from 10 to 45 microns, at a pressure of 60 to 80 psi. After grit-blasting, native oxide layer was removed from the implant surfaces by placing 4 implants in 100 ml. of a 15% solution of HF in water at room temperature for 30 seconds. The  
20     implants were then removed from the acid, neutralized in a solution of baking soda, and placed in 150 ml. of "Modified Muriaticetch" (described above) at room temperature for 3 minutes. The implants were then removed from the acid, neutralized, rinsed and cleaned. All samples displayed very similar surface topographies and a high level of etch uniformity over the surface, when compared  
25     with each other in SEM evaluations. Consistency in the surface features (peaks and valleys) was also observed. The SEMs in FIGS. 5A, 5B, 6A and 6B show the surfaces of two of the implants, Sample A-1 and Sample A-4, at magnifications of 2,000 and 20,000. It will be observed that the surface features over the areas shown are consistent and uniform. The scale shown on the X20,000 photographs is 1  
30     micron = 0.564 inch. At this magnification the surfaces appear to be characterized by a two-dimensional array of cones ranging in height (as seen in the SEMs) from about 0.17 inch to about 0.27 inch; the base diameters of these cones varied from

about 0.17 inch to about 0.33 inch. Converting these numbers to metric units on the above-mentioned scale (1 micron = 0.564 inch) yields:

cone height range (approx.) = 0.30 to 0.50 micron

cone base diameter range (approx.) = 0.30 to 0.60 micron.

- 5 The same degree of uniformity was found in all the samples, and from sample to sample, at magnifications of 2,000 and 20,000, as compared with similar samples subjected to bulk etching without prior removal of the native oxide, as described in EXAMPLE NO. 2 below.

#### EXAMPLE NO. 2

- 10 Four of the implants that had been grit blasted as described in EXAMPLE NO. 1 above were placed in 150 ml. of "Modified Muriaticetch" for 10 minutes. The implants were then removed, neutralized, rinsed and cleaned. SEM photographs taken at magnifications of 2,000 and 20,000 showed that the bulk etch solution failed to remove the native oxide layer after 10 minutes in the etch solution. The failure to  
15 remove the native oxide layer (100-150 Angstrom units thick) resulted in a non-uniformly etched surface, as depicted in FIG. 3. In areas of the implant surfaces where the native oxide was removed, the topography was similar to that observed on the implants in EXAMPLE NO. 1.

#### EXAMPLE NO. 3

- 20 The procedure of this example is currently preferred for producing commercial implants. A batch of screw-type implants made of CP titanium were immersed in a 15% solution of HF in water at room temperature for 60 seconds to remove the native oxide layer from the implant surfaces. A plastic cap was placed over the top of each implant to protect it from the acid. The implants were then  
25 removed from the acid and rinsed in a baking soda solution for 30 seconds with gentle agitation. The implants were then placed in a second solution of baking soda for 30 seconds, again with agitation of the solution; and then the implants were rinsed in deionized water. Next the implants were immersed in another solution of two parts by volume sulfuric acid (96% by weight H<sub>2</sub>SO<sub>4</sub>, 4% by weight water) and one part by volume hydrochloric acid (37% by weight HCl, 63% by weight water) at  
30 70°C for 5 minutes. The implants were then removed from the acid and rinsed and neutralized by repeating the same steps carried out upon removal of the implants

from the HF. All samples displayed very similar surface topographies and a high level of etch uniformity over the surface, when compared with each other in SEM evaluations. Consistency in the surface features (peaks and valleys) was also observed. The SEMs in FIGS. 8A, 8B, 9A and 9B show the surfaces of two of the implants, Sample 705MB and Sample 705MC, at magnifications of 2,000 and 5 20,000. It will be observed that the surface features over the areas shown are consistent and uniform. The scale shown on the X20,000 photographs is 1 micron = 0.564 inch. At this magnification the surfaces appear to be characterized by a two-dimensional array of cones ranging in height (as seen in the SEMs) from about 0.17 10 inch to about 1.128 inch; the base diameters of these cones varied from about 0.17 inch to about 1.128 inch. Converting these numbers to metric units on the above-mentioned scale (1 micron = 0.564 inch) yields:

cone height range (approx.) = 0.30 to 0.20 microns

cone base diameter range (approx.) = 0.30 to 0.20 microns.

15 The same degree of uniformity was found in all the samples, and from sample to sample, at magnifications of 2,000 and 20,000, as compared with similar samples subjected to bulk etching without prior removal of the native oxide, as described in EXAMPLE NO. 2 above.